For Boston 2011 SETAC meeting, Invited Platform Talk

Cross-Species Extrapolation of EDC Toxicity: Consequences for Screening Programs. Gerald Ankley, USEPA, NHEERL, MED, Duluth, MN, USA.

Many structural and functional aspects of the vertebrate hypothalamic-pituitary-gonadal (HPG) axis are known to be highly conserved, but the full significance of this from a toxicological perspective has received comparatively little attention. High-quality data generated through development and validation of different Tier 1 tests for the USEPA Endocrine Disruptor Screening Program (EDSP) offer a unique opportunity to compare responses of mammals versus fish to chemicals that affect different pathways within the HPG axis. This analysis used data from 12 different chemicals that act as estrogen receptor agonists (17α-ethynylestradiol, methoxychlor, Bisphenol A), androgen receptor agonists (methyltestosterone, 17β-trenbolone), androgen receptor antagonists (flutamide, vincolozolin, p,p'-DDE) or inhibitors of different steroidogenic enzymes (ketoconazole, fadrozole, fenarimol, prochloraz) that had been tested in the 21-d fathead minnow assay and in one or more of the other four in vivo (rat) Tier 1 screens (Uterorophic, Hershberger, male and female pubertal assays). Each of the 12 chemicals was identified as endocrine-active by two or more of the five Tier 1 assays, indicating excellent coverage of the HPG pathways of concern. The fathead minnow assay was positive for all the test chemicals. The consequences of these observations in terms of screening efforts like the USEPA EDSP will be discussed.